Docket No. MWH-0031US *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Stephen B. Liggett
Application No.:	09/936,499
Filed:	December 17, 2001 (35 U.S.C. § 371 of PCT/US00/06502, filed March 10, 2000, which claims benefit of U.S. Appl. No. 60/124,060, filed March 12, 1999)
Confirmation No.:	4401
Group No.:	1634
Examiner:	Goldberg, J.
For:	**VARIATION IN DRUG RESPONSE RELATED TO POLYMORPHISMS IN BETA 2-ADRENERGIC RECEPTOR**

Commissioner for Patents
Washington, D.C. 20231

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REQUEST FOR RECONSIDERATION/WITHDRAWAL OF RESTRICTION REQUIREMENT UNDER 37 C.F.R. § 1.143

This paper is being submitted in response to the Office Action dated March 25, 2003, wherein the Examiner (1) asserts that the captioned application contains three distinct groups of inventions (Group I: claims 1-5; Group II: claims 6-10; and Group III: claims 11-14) that are not so linked as to form a single general inventive concept under PCT Rule 13.1, and (2) requires Applicant to elect, in accordance with 37 C.F.R. § 1.499, a single invention to which the claims must be restricted. Applicant respectfully disagrees with the Examiner's assertion, and requests withdrawal of the restriction requirement.

At the outset, Applicant reminds the Examiner that the correct standard for restricting among groups of inventions in a 35 U.S.C. § 371 application is the existence of "unity of

invention" among the groups of inventions. 37 C.F.R. § 1.475. Where a group of inventions is claimed in such an application, the requirement of unity of invention is satisfied when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. *Id.* The phrase "special technical features" are those that define a contribution which each of the claimed inventions, considered as a whole, make over the prior art. *Id.*

Because there is a technical relationship among the inventions of Groups I, II, and III involving one or more of the same or corresponding special technical features, Applicant submits that the inventions of Groups I, II, and III are indeed linked so as to form a general inventive concept.

The invention of Group I (claims 1-5) is directed to a method for predicting an individual's bronchodilating response to an agonist of β_2AR comprising determining the individual's genotype for the +491 polymorphic site, wherein a heterozygous C/T genotype or a homozygous T/T genotype indicates that the individual is likely to exhibit a poor bronchodilating response to the agonist. The invention of Group II (claims 6-10) is directed to methods for predicting a patient's bronchodilating response to an agonist of β_2AR comprising assaying a sample from the patient for expression of the Ile164 β_2AR variant, wherein the presence of the Ile164 β_2AR variant indicates the patient is likely to exhibit a poor bronchodilating response to the agonist. The invention of Group III (claims 11-14) is directed to methods for treating a patient suffering from asthma or COPD comprising determining the patient's genotype for the +491PS and making a treatment decision based on the genotype, wherein if the patient has a heterozygous C/T genotype or a homozygous T/T genotype, the treatment decision is selected from the group consisting of: (a) prescribing a higher dose of a β-agonist than typically indicated for individuals having similar weight and symptoms; (b) prescribing more frequent doses of a β-agonist than typically indicated for individuals having

similar weight and symptoms; (c) prescribing both a higher dose and more frequent doses of a β-agonist than typically indicated for individuals having similar weight and symptoms; (d) not prescribing a β-agonist; and (e) prescribing a β-agonist in conjunction with another bronchodilating therapy.

As can be clearly seen, with respect to these groups of inventions, the shared special technical feature is that there is variation in the human population with respect to nucleotide position +491 of the β_2AR gene (there are alleles of this gene), and that this variation is related to the activation of β_2AR by β_2AR agonists. Applicant has demonstrated that when a given individual possesses a genotype of C/T or T/T with respect to position +491 of the β_2AR gene, the individual is likely to exhibit a poor bronchodilating response to β_2AR agonists (claims 1-5). These genotypes correspond with the presence of isoleucine (Ile) at amino acid position 164 of β_2AR. Thus, when a given individual possesses an Ile164 β_2AR variant, the individual is likely to exhibit a poor bronchodilating response to β_2AR agonists (claims 6-10). Finally, if the individual possesses a genotype of C/T or T/T with respect to position +491 of the β_2AR gene, and such individual suffers from asthma or COPD, then because either of these genotypes is predictive of the individual exhibiting a poor bronchodilating response to β_2AR agonists, the individual can be treated with this fact in mind, meaning (a) prescribing a higher dose of a β-agonist than typically indicated for individuals having similar weight and symptoms; (b) prescribing more frequent doses of a β-agonist than typically indicated for individuals having similar weight and symptoms; (c) prescribing both a higher dose and more frequent doses of a β-agonist than typically indicated for individuals having similar weight and symptoms; (d) not prescribing a β-agonist; and (e) prescribing a β-agonist in conjunction with another bronchodilating therapy (claims 11-14).

In view of the foregoing, Applicants respectfully submit that there is a shared special technical feature among the inventions of Groups I, II, and III, and therefore requests withdrawal of the restriction requirement. In the event that Applicant's request for withdrawal of the restriction requirement is denied, Applicant elects to prosecute the invention of Group I (claims 1-5).

Respectfully submitted,

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